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## DIPHTHERIA IMMUNIZATION.

In recent years there has come into use a practical method for testing immunity to diphtheria known as the Schick test, similar to the test with vaccine virus for immunity to smallpox, and also a method for conferring on children permanent immunity to diphtheria by the injection of diphtheria toxin-antitoxin mixture. The introduction of these methods into America, and a more extensive application than has hitherto been practiced in any country, are due to the workers of the laboratory of the New York City department of health, of which Dr. W. H. Park is the head.

### The Schick Test for Immunity to Diphtheria.

The Schick test consists in the intracutaneous (not subcutaneous) injection of a small amount of diluted diphtheria toxin, a positive reaction being shown by a red papule and indicating that the subject tested has not enough antitoxin in his blood to ward off an attack of diphtheria. In this test, therefore, a reaction indicates nonimmunity. In healthy young adults somewhat less than half may be expected to give positive reactions; in children there is a larger proportion of susceptibles.

*Purpose.*—The test is useful (a) in determining the susceptibles (those with positive Schick reactions) to be immunized with a toxin-antitoxin mixture, in case more permanent protection is desired, or with antitoxin instead, if there is immediate danger of infection; and (b) in indicating that carriers of the diphtheria bacillus who happen to have slight throat symptoms, but who have given a negative Schick reaction, are not suffering from diphtheria.

*Toxin.*—The classical dose for the Schick test is one-tenth cubic centimeter of a toxin diluted so that this amount contains one-fiftieth of a minimal lethal dose for guinea pigs. Zingher, in New York, has recently used two-tenths cubic centimeter of a weaker dilution which contains one-fortieth of a minimal lethal dose in this double volume. In practice it is safer to add some such excess (25 per cent) on account of the deterioration which diphtheria toxin undergoes and to avoid interpreting a weak positive reaction as a negative. Minimal lethal doses are not readily determined and delivered with much greater accuracy than that represented by 25 per cent differences. Although only those toxins should be used which are sufficiently aged to be relatively stable, it is well to remember that diphtheria toxin is subject to loss in toxicity, especially when diluted, that the dilution

should not be made more than 12 hours before use, and that the toxin should at all times be kept in the coldest part of the ice box.

*Control.*—Since pseudoreactions may be caused by the proteins in the toxin broth and not by the true toxin, each test should be controlled by the injection, at a corresponding site on the other arm, of the same amount of similarly diluted toxin which has been heated to 75° C. for 10 minutes in order to destroy its specific toxic properties. It is advised that two test injections and two control injections be made, four in all; more definite readings are thus obtained. Pseudoreactions appear earlier and do not last as long as true reactions.

*Instruments.*—Two tuberculin syringes are needed so graduated that the dose of one-tenth cubic centimeter may be easily and accurately measured; one of these should be plainly marked and used for the unheated toxin, the other for the control. The needles, being boiled between injections, may be used interchangeably on either syringe. The needles should be of fine caliber (about 26-gauge) and kept very sharp. They are most easily manipulated if fairly short (one-fourth to one-half inch) and with a bevel not too tapering.

*Technique.*—With the usual sterile precautions, one-tenth cubic centimeter (or one-fifth cubic centimeter if the New York dilution is used) of the unheated toxin dilution is introduced intracutaneously (not subcutaneously) on the flexor surface of the right forearm, and the same amount of the control dilution on the flexor surface of the left forearm. The needle should be inserted parallel with the skin surface, far enough to avoid leakage backward along the needle track, and deep enough so that the oval opening of the needle is just visible through the epidermis. If the injection is at the proper depth it will form a white elevation in which the depressions of the hair follicles are prominent.

*Reading.*—A red area at least one-fourth inch in diameter on the right arm, distinctly more marked in 96 hours than the area on the left arm, may be taken as a positive reaction. If two injections are made on each arm, the variation in reaction caused by injecting one of the dilutions deeper than the other is balanced. The amount of discoloration where the heated toxin was injected indicates the degree of pseudoreaction.

#### **Diphtheria Toxin-Antitoxin Mixture.**

Active immunization of young children against diphtheria is useful in institutions, and in localities where prompt diagnosis and treatment of diphtheria are not assured. The most favorable age for active immunization is from six months to six years. In older children and in adults a considerable proportion of pseudoreactions to the Schick test, which offer difficulty in interpretation, may be expected, with correspondingly greater local and constitutional reactions fol-

lowing the injection of toxin-antitoxin mixture. Active immunization can not be used instead of passive immunization with antitoxin in the presence of actual exposure to diphtheria, since the active immunity is slow in developing; neither should a combination of the two methods be used simultaneously, since the 1,000 units of antitoxin used for passive immunization tends to prevent the development of immunity from the toxin-antitoxin mixture, if both are injected at about the same time.

The toxin-antitoxin mixture used in active immunization is not quite neutralized, large doses injected into guinea pigs producing some reaction; this remaining toxicity is necessary in order to stimulate the production of immunity. Only such reactions occur as are observed after typhoid immunization. In older persons who give pseudoreactions to the Schick test, a certain amount of local and constitutional disturbance may be expected. In general, young children bear the injection without any marked disturbance.

By the Schick test for the presence, or rather absence, of natural antitoxin in the patient it is found that only a certain proportion of persons are susceptible to diphtheria, therefore before active immunization a Schick test should be performed in the case of older children, and only those giving positive reactions should receive the toxin-antitoxin mixture. Children under two years of age are so generally susceptible to diphtheria that the preliminary Schick test may be omitted in their case.

As for typhoid immunization, three doses should be injected subcutaneously at about weekly to two-weekly intervals. These doses are usually 1 cubic centimeter in volume.

Six months after the first series of injections another Schick test should be performed and the few who have not developed by that time an immunity which is shown by a negative Schick reaction should receive a second series of injections with the toxin-antitoxin mixture.

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## A REPORT ON THE SECOND ENGLISH-SPEAKING CONFERENCE ON INFANT WELFARE.

By TALIAFERRO CLARK, Surgeon, United States Public Health Service.

The Second English-Speaking Conference on Infant Welfare was held in London, England, July 5-7, 1921, under the auspices of the National League for Health, Maternity, and Child Welfare, and was attended by approximately 600 delegates representing 26 English-speaking countries. The United States Public Health Service, the American Public Health Association, and the American Child Hygiene Association were represented by the writer.

The conference was held during the celebration of the National Baby Week, 1921, in connection with which an interesting display of the latest exhibits and posters relating to the welfare of mothers and babies had been prepared. This exhibit and also daily demonstrations on the care of the baby and free consultations and advice on the health of mothers and young children were available to visiting delegates. In addition, throughout the period of the con-